184 Hematuria

WANDA G. KIRKPATRICK

Definition

Hematuria is blood in the urine. Hematuria is termed *gross*, or *macroscopic*, when there is sufficient blood present to color the urine red or brown. Hematuria is termed *microscopic* when the urine is visually normal in color but is found to contain blood on chemical analysis or microscopic evaluation.

Technique

Evaluation of the patient with hematuria should begin with a careful history. The pattern of hematuria and its associated symptoms should be elicited (i.e., gross vs. microscopic, constant vs. intermittent, and painless vs. painful). Important historical findings include fever, back pain, dysuria, urgency, frequency (urinary tract infection); renal colic or previous nephrolithiasis (renal stone disease); weight loss, especially with abdominal pain (renal cell carcinoma); or weight loss with a significant smoking history, analgesic abuse, or exposure to industrial dyes (bladder carcinoma); recent sore throat or skin infection, edema, hypertension (glomerulonephritis); recent back, abdominal, or urethral injury or vigorous exercise (trauma); history of heart murmur with recent dental or genitourinary manipulation (endocarditis); or a history of bleeding from other sites, a previous bleeding disorder, or family history of a bleeding disorder (systemic coagulopathy).

A careful drug history should be taken with special attention to analgesics (papillary necrosis), cyclophosphamide (hemorrhagic cystitis), anticoagulants, and drugs known to cause acute interstitial nephritis (see Table 184.1).

A personal or family history of hematuria with deafness or ocular abnormalities (Alport's syndrome), or hematuria with progressive chronic renal failure (polycystic kidney disease), should be sought, as well as a family history of sickle hemoglobin.

Finally, a careful travel history should be obtained because Schistosoma haematobium is a common cause of hematuria in certain endemic areas.

On physical examination, vital signs should be checked with special attention to blood pressure and temperature. The skin should be examined carefully for rash, ecchymoses, or petechiae. Lens abnormalities and hearing loss should be noted. Cardiac murmurs, rales, costovertebral angle tenderness, abdominal tenderness, and abdominal masses are important findings. Genital examination should include investigation for possible sites of bleeding around the urethral meatus in both sexes or vaginal bleeding in the female.

When the history and physical examination are complete, a careful urinalysis should be performed by the physician. A number of substances other than blood may color the urine red, including porphyrins, phenazopyridine (Pyridium), beets, free hemoglobin, and myoglobin. In addition, the standard dipstick using orthotoluidine reagent to detect blood will be positive in the presence of either free hemoglobin or myoglobin. Therefore hematuria should be confirmed by the presence of red blood cells on microscopic examination.

After documenting that hematuria is present, a careful search for other urinary abnormalities is helpful. The presence of proteinuria suggests a renal parenchymal etiology and should be quantified by timed urine collection. Urine protein excretion of greater than 1g/24 hr is virtually diagnostic of renal parenchymal disease. Urine protein excretion of less than 1 g/24 hr is not helpful in the differential diagnosis because it may be due simply to the presence of serum proteins that accompany the hematuria, or protein released from red cells that have lysed.

White cells or white cell casts may accompany red cells in infectious or noninfectious inflammation (e.g., acute interstitial nephritis or acute glomerulonephritis). Red blood cell casts are diagnostic of a renal etiology of hematuria, usually glomerular in origin. Crystals may be seen in patients with nephrolithiasis, but many types of crystals may also be present in the urine of patients without renal stones.

In addition to a complete urinalysis, a complete blood count, serum electrolytes, blood urea nitrogen, and serum creatinine should be obtained. In patients with evidence of infection, urine culture should be obtained. If there is suspicion of a coagulation disturbance, a prothrombin time, partial thromboplastin time, and bleeding time should be

Table 184.1
Drugs Associated with Acute Interstitial Nephritis

Antibiotics
Penicillins (esp. methicillin, ampicillin)
Cephalosporins
Sulfonamides
Rifampin
Isoniazid
Nonsteroidal anti-inflammatory drugs
Indomethacin
Phenylbutazone
Fenoprofen
Naproxen
Tolmetin
Mefenamic acid
Diuretics
Thiazides
Furosemide
Triamterene
Miscellaneous
Phenytoin
Cimetidine
Allopurinol
Azathioprine

checked. Black patients should be screened for the presence of sickle hemoglobin because of the high prevalence of hematuria in patients with sickle trait. If there is a history of renal colic, a kidney/ureter/bladder examination should be performed to look for a renal stone, followed by excretory urography if appropriate. If there is a history suggestive of malignancy, cystoscopy should be performed to evaluate for bladder tumors; abdominal computerized tomography or renal arteriography should be done if renal tumor is suspected.

If an obvious source is not apparent after the initial evaluation, then excretory urography should be done. Cystoscopy should be performed in patients with gross hematuria, findings suggestive of a lower tract source of bleeding and in all older men. The efficacy of routine cystoscopy for asymptomatic microscopic hematuria in women and men under the age of 40 has been questioned and is probably not warranted on a routine basis. A skin test for tuberculosis should be placed and, if positive, first-voided morning urine specimens for mycobacterial culture should be obtained on three different occasions to rule out genitourinary tuberculosis. If all other evaluation is nondiagnostic, or if there is evidence of renal parenchymal disease, nephrologic consultation should be obtained for consideration of percutaneous renal biopsy.

Table 184.2
Differential Diagnosis of Hematuria

Acquired glomerular and tubulointerstitial renal disease
Primary
Secondary to systemic disease
Hereditary renal disease
Alport's syndrome
Polycystic kidney disease
Infection (including Mycobacteria and Schistosoma)
Papillary necrosis
Sickle hemoglobin
Analgesic abuse
Diabetes mellitus
Trauma
Calculi
Neoplasia
Primary
Metastatic (uncommon)
Coagulopathy
Congenital
Acquired

Basic Science

Red blood cells may be excreted in the urine by normal persons. It is not known precisely how these cells reach the urinary tract. However, the normal excretion rate is 0.5 to 2 million RBCs/24 hr, or less than 5 RBCs/hpf on microscopic examination of a spun urine specimen.

It is difficult to localize the site of bleeding by routine examination of the patient with hematuria. However, certain findings may be very helpful. For example, casts form in the lumina of renal tubules. Therefore, the presence of red blood cell casts localizes the site of bleeding to the renal parenchyma. Red cell morphology examined under phase contrast microscopy may also be helpful because red cells of glomerular origin tend to be distorted with variation in size and shape. This is thought to result from the red cells' passage through the nephron. In contrast, red cells of nonglomerular origin generally maintain uniform size and characteristic shape. Red blood cell size distribution curves measured with an automated analyzer may also reflect the distortion of red cells that occurs as they traverse the nephron. In "glomerular" hematuria, urinary RBCs have an irregular size distribution and tend to be smaller than peripheral RBCs. In "nonglomerular" hematuria, urinary RBCs are more uniform in size distribution and have a larger mean volume with the peak volume being greater than that of peripheral RBCs.

Clinical Significance

Hematuria may be caused by a large number of diverse disease processes most of which are not life threatening. However, a number of clinical studies have shown that the incidence of serious diseases manifest as hematuria is of adequate magnitude to justify investigation of virtually all patients. Despite careful evaluation, approximately 10–15% of patients will have no apparent cause found and generally have an excellent prognosis.

References

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